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EXAMINER	
LAU, JONATHAN S	
ART UNIT	PAPER NUMBER
1623	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,001	JENKINS, JOHN	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *4-7, 11, 12, 17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8-10,13-16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5 pgs / 13 Jun 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is the national stage entry of PCT/GB03/01613, filed 15 Apr 2003; and claims benefit of foreign priority document UNITED KINGDOM 0208516.5, filed 15 Apr 2002. The foreign priority document is in English.

Claims 1-19 are pending in the current application. Claims 3-7, 11, 12, 17 and 18 drawn to non-elected species, are withdrawn. Claims 1, 2, 8-10, 13-16 and 19 are examined on the merits herein.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-19, in the reply filed on 06 Jun 2008 is acknowledged. Claims 20-31, are canceled. The traversal on the ground(s) that claims are limited to a reasonable number of species and each species are part of a same respective genus is not relevant to the restriction requirement between Groups I-V.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of species with traverse of a first agent of gemcitabine and a second agent of 17-methoxygeldanamycin and the second species of bowel cancer in the reply filed on 06 Jun 2008 is acknowledged. The traversal is on the ground(s) that claims are limited to a reasonable number of species and each species are part of a same respective genus. This is not found persuasive because the measure of a reasonable number of species is in part determined based on the diversity and

complexity of the genus, the genus of compounds that have distinct chemical structures and distinct physiological modes of action and the genus of diseases with distinct etiologies and methods of treatment.

Applicants identify 17-methoxygeldanamycin as reading upon claim 11, however it is found that 17-methoxygeldanamycin is synonymous with geldanamycin, which has a methoxy group at the 17 position (see instant specification, page 10). Accordingly, claim 11 is withdrawn, and claim 10 reciting geldanamycin is examined on the merits.

Claims 3-7, 11, 12, 17 and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the election of species requirement in the reply filed on 06 Jun 2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 8-10, 13-16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 2, 9, 10, 13-16 and 19 claim a first agent defined by functional properties of said first agent recited in claims 1 and 2, claim 1: "a first agent that attenuates Topoisomerase I (Topo I) activity" and claim 2: "the first agent is a compound selected from the group consisting of: (i) compounds that bind to Topo I and inhibit its activity, (ii) compounds which prevent the transcription, translation or expression of Topo I, (iii) compounds which inhibit release of Topo I from intracellular stores, and (iv) compounds which increase the rate of degradation of Topo I". Claim 8 recites a specific chemical compound capable of performing such functional properties. The specification at pages 7-9 discloses specific chemical compound embodiments of said first agent.

Claims 1, 2, 8, 9, 13-16 and 19 claim a second agent defined by functional properties of said second agent recited in claims 1 and 9, claim 1: "a second agent that inhibits Heat Shock Protein 90 (HSP90) activity" and claim 9: "the second agent is a compound selected from the group consisting of: (i) compounds that bind to HSP 90 and inhibit its activity, (ii) compounds which prevent the transcription, translation or expression of HSP 90, (iii) compounds which inhibit release of HSP 90 from intracellular stores, and (iv) compounds which increase the rate of degradation of HSP 90". Claim 10 recites a specific chemical compound capable of performing such functional properties. The specification at pages 9-11 discloses specific chemical compound embodiments of said second agent.

Functional language, as herein employed by Applicants, is admonished in University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (CAFC, 1997). The CAFC states that "[A] written description of an invention involving a chemical genus, like a

description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result." at 1406 (emphasis added).

Thus, Applicants functional language fails to meet the written description requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (General Electric Company v. Wabash Appliance Corporation et al. 37 USPQ at 468 (US Supreme Court 1938)).

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art

cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in University of California v. Eli Lilly and Co. Hence, in the absence of fully recognizing the identity of the members of the genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions used in the claimed methods herein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 8-10, 13-16 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 9, 10, 13-16 and 19 claim a first agent defined by functional properties of said first agent recited in claims 1 and 2, claim 1: “a first agent that attenuates Topoisomerase I (Topo I) activity” and claim 2: “the first agent is a compound selected from the group consisting of: (i) compounds that bind to Topo I and inhibit its activity, (ii) compounds which prevent the transcription, translation or expression of Topo I, (iii) compounds which inhibit release of Topo I from intracellular stores, and (iv) compounds which increase the rate of degradation of Topo I”. Claim 8 recites a specific chemical compound capable of performing such functional properties.

Claims 1, 2, 8, 9, 13-16 and 19 claim a second agent defined by functional properties of said second agent recited in claims 1 and 9, claim 1: "a second agent that inhibits Heat Shock Protein 90 (HSP90) activity" and claim 9: "the second agent is a compound selected from the group consisting of: (i) compounds that bind to HSP 90 and inhibit its activity, (ii) compounds which prevent the transcription, translation or expression of HSP 90, (iii) compounds which inhibit release of HSP 90 from intracellular stores, and (iv) compounds which increase the rate of degradation of HSP 90". Claim 10 recites a specific chemical compound capable of performing such functional properties.

Claims 1, 2, 8-10, 13-16 and 19, drawn to both a first agent and a second agent, are indefinite for failing to particularly point out and distinctly claim both said first agent and said second agent. One of skill in the art would not be reasonable apprised of the metes and bounds of the claims, such as the chemical composition required of said first agent and said second agent based on the functional properties defining said first agent and said second agent.

As recited above, functional language, as herein employed by Applicants, is admonished in University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (CAFC, 1997). The CAFC states that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what

the gene does, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result." at 1406.

Therefore claims 1, 2, 8-10, 13-16 and 19 are indefinite for failing to particularly point out and distinctly claim the subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 8-10, 13-16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosen et al. (US Patent 7,211,562, PCT filed 01 Nov 2001, cited in PTO-892) in view of Sugarbaker (Cancer Chemother Pharmacol, 1999, 43(Suppl), pS15-S25, cited in PTO-892).

Rosen et al. teaches combination therapy comprising the administration of cytotoxic agents followed by administration of heat shock protein 90 (HSP90) inhibitors for the treatment of an animal that has a cell proliferative disorder to allow the use of a lower dose of the cytotoxic agent (abstract). Rosen et al. teaches the combination wherein the cytotoxic agent is selected from gemcitabine (column 13, lines 5-10), a compound which prevents the transcription, translation or expression of Topo I. Rosen et al. teaches the HSP90 inhibitor geldanamycin (column 3, lines 22-23). Rosen et al.

teaches the method of administration for inhibition of growth of cells causing a cell proliferative disorder (column 7, lines 50-52), which is interpreted as a treatment encompassed within the scope of prophylatic treatment. Rosen et al. teaches a need for cancer treatments which target specific cancer types (column 4, lines 40-45).

Rosen et al. does not specifically disclose the embodiment of the combination of gemcitabine and geldanamycin. Rosen et al. does not specifically disclose the method for the treatment of bowel cancer. Rosen et al. does not specifically disclose the method for the treatment of bowel cancer as a paediatric tumor.

Sugarbaker teaches gemcitabine is in routine clinical use in patients with peritoneal seeding from surface spread of large bowel cancer (page S19, left column, paragraph 3 and right column, paragraph 3).

It would have been obvious to one of ordinary skill in the art to combine Rosen et al. with the teaching of Sugarbaker. Both Rosen et al. and Sugarbaker are in the field of management of cell proliferative disorders. One of ordinary skill in the art would be motivated to select the combination of gemcitabine and geldanamycin because Rosen et al. provides guidance for using the specific cytotoxic agent gemcitabine and because Rosen et al. teaches a need for cancer treatments which target specific cancer types. One of ordinary skill in the art would be motivated to treat the specific cell proliferative disorder of bowel cancer because Sugarbaker teaches gemcitabine is in routine clinical use in patients with peritoneal seeding from surface spread of large bowel cancer. It would have been obvious to one of ordinary skill in the art to perform the method for the treatment of bowel cancer as a paediatric tumor. Rosen et al. teaches it is well within

the level of ordinary skill in the art to administer the treaterment according to the requirements of the patient according to age, condition and size of the patient (Rosen et al. column 14, lines 10-20).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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